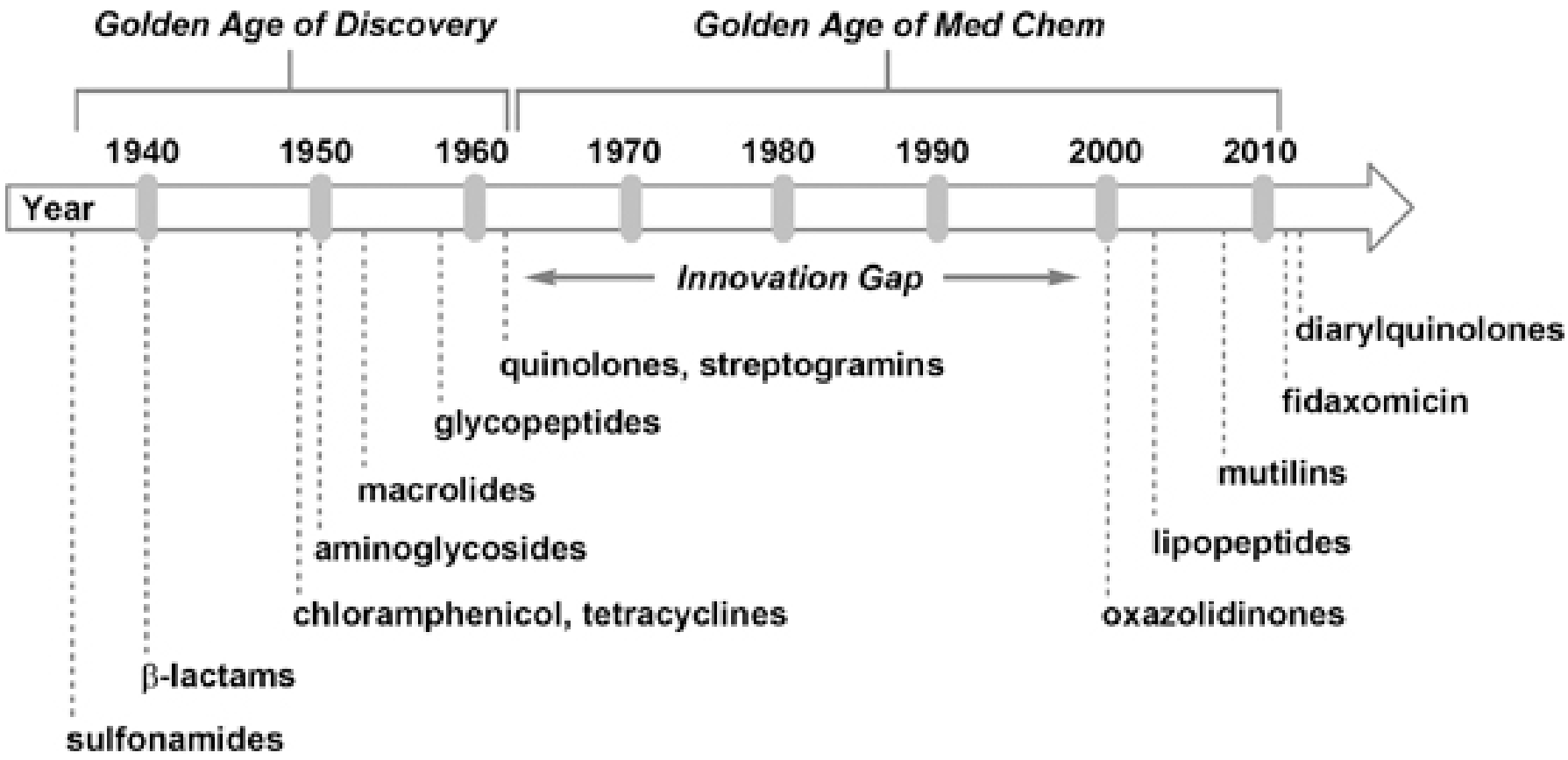
Antibiotika
(Antimikrobielle midler)

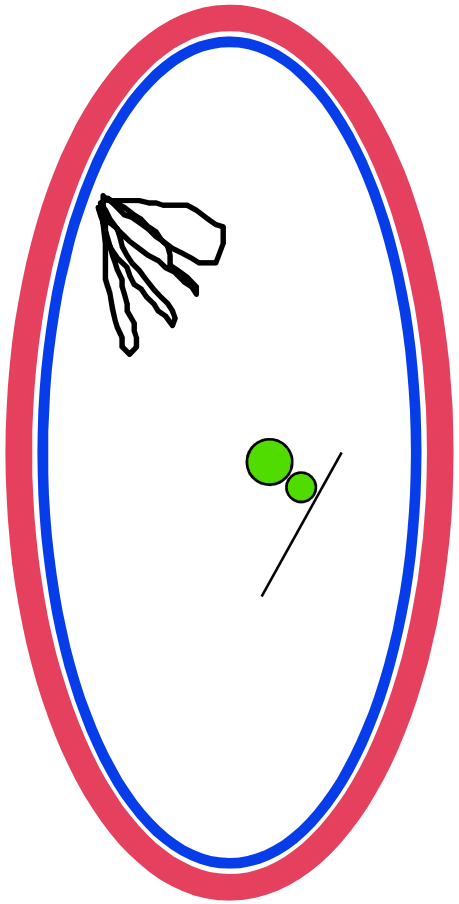
Antibiotika- Defenition

Kemiske forbindelser produceret af mikroorganismer, der er i stand til at dræbe eller forhindre vækst af bakterier eller andre mikroorganismer

Opdagelse af antibiotika

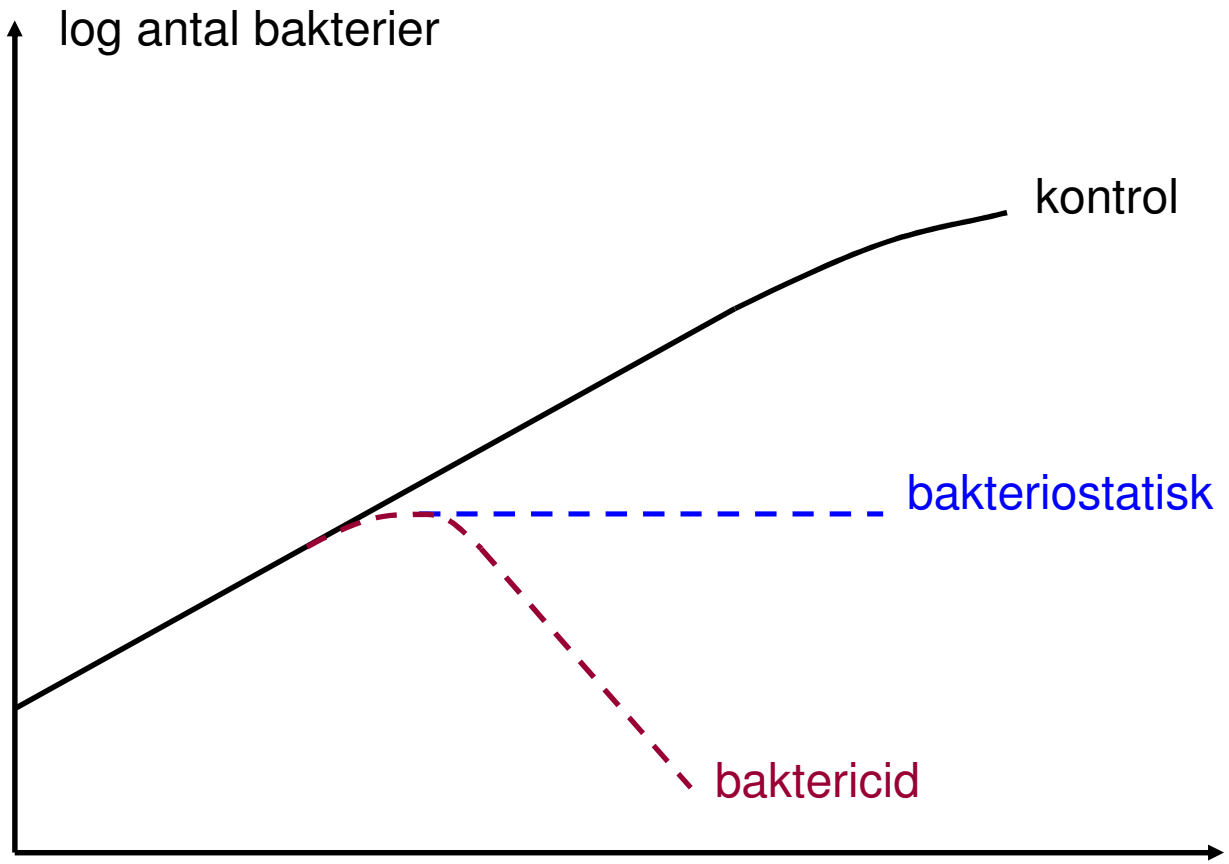


Antimicrobials - Mode of Actions



- Cell wall
  - penicillins, cephalosporins
- Cytoplasm membrane
  - polymyxins
- Protein synthesis
  - aminoglycosides, tetracycline's, macrolides, amphenicols
- DNA
  - sulphonamides, TMP, BQP, fluoroquinolones

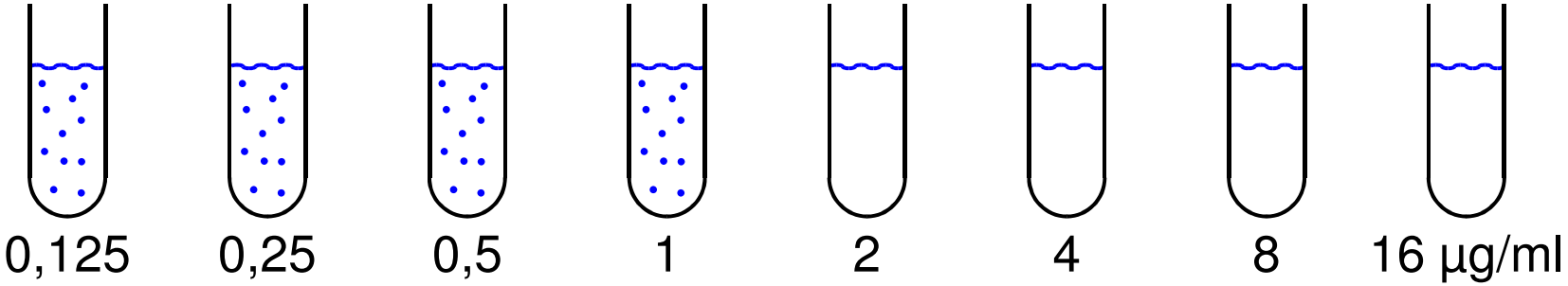
Drabskurver



MIC-værdi
(minimal inhibitory concentration)

Den mindst hæmmende koncentration af et antibiotikum overfor en given mikroorganisme målt i µg/ml.

MIC-bestemmelse



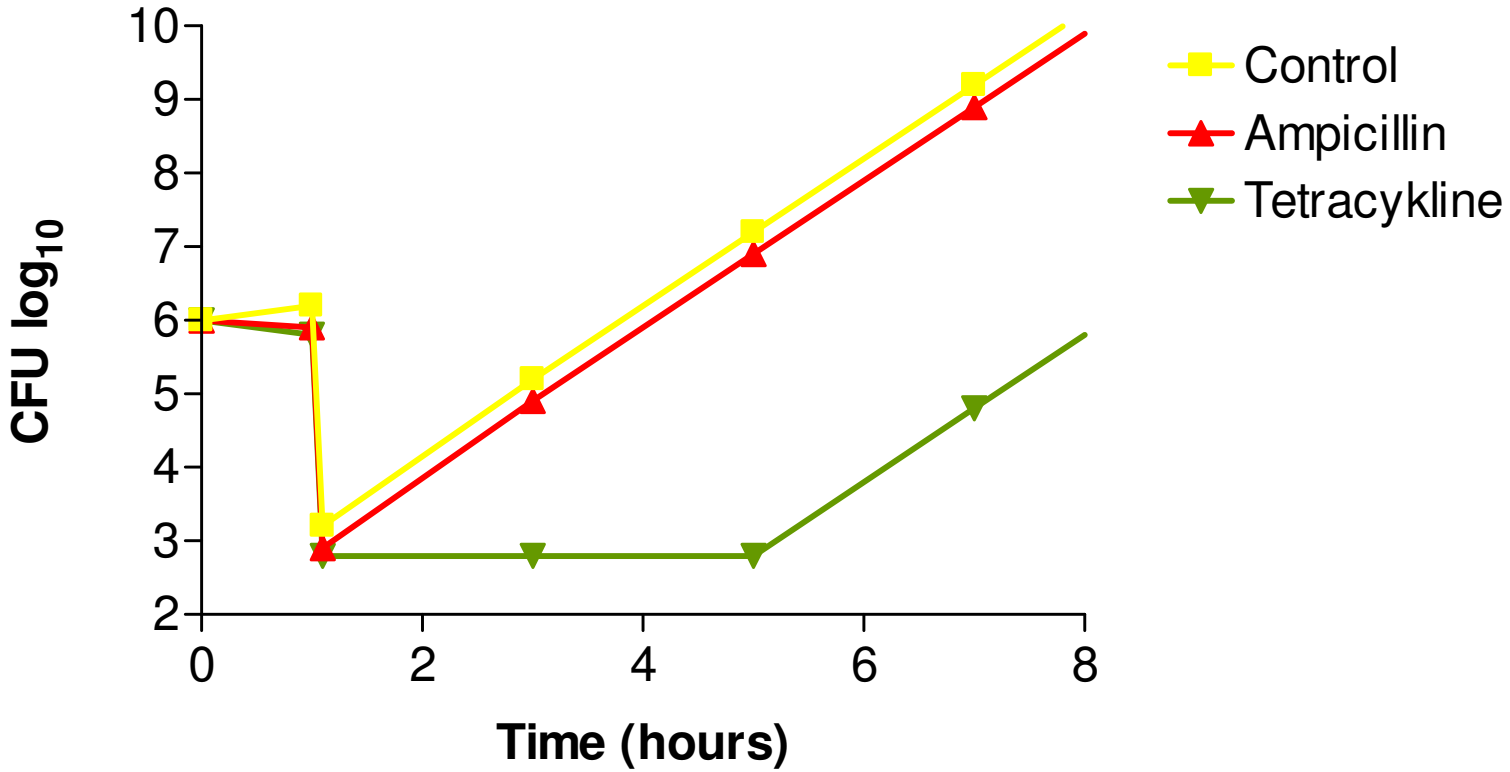
Faktorer, der påvirker MIC:

1. Inoculum
2. Medium
3. Inkubationstid

MIC-bestemmelsen tager ikke højde for:

1. Baktericide effekt af serum komponenter
2. Øget fagocytose af defekte bakterier
3. Ændringer af pH i inflammationsfoci

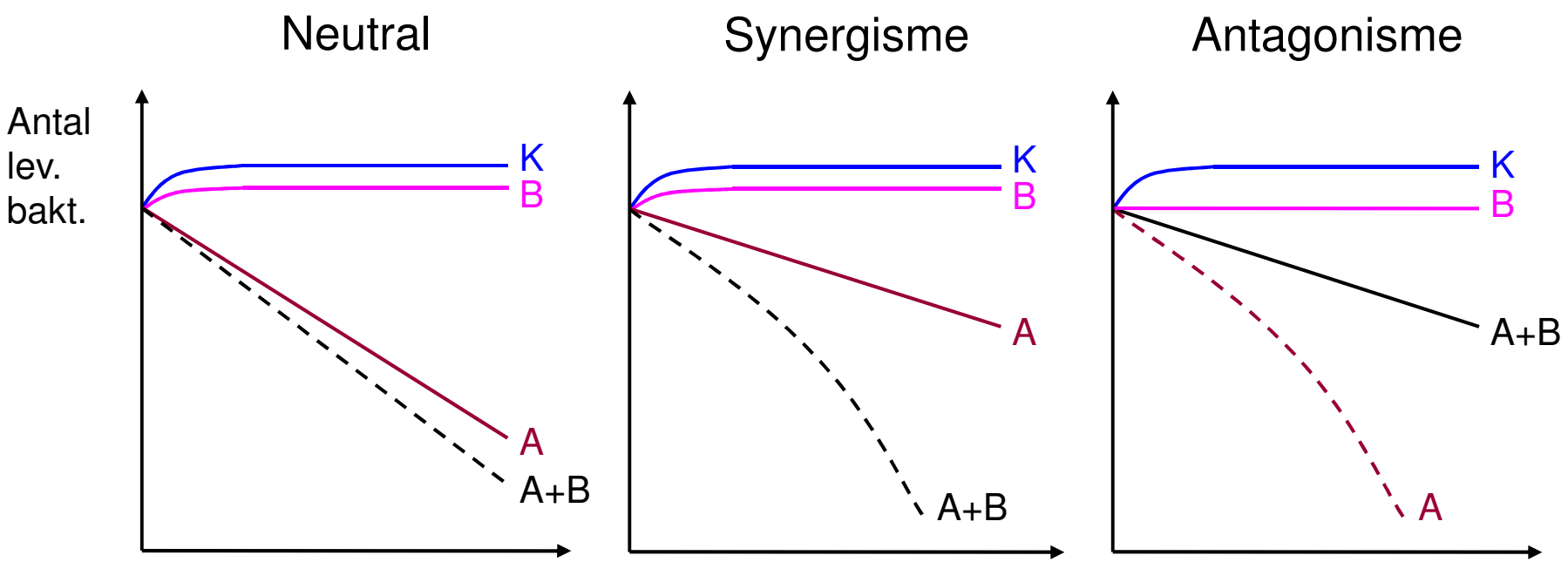
Postantibiotic effect, E. coli



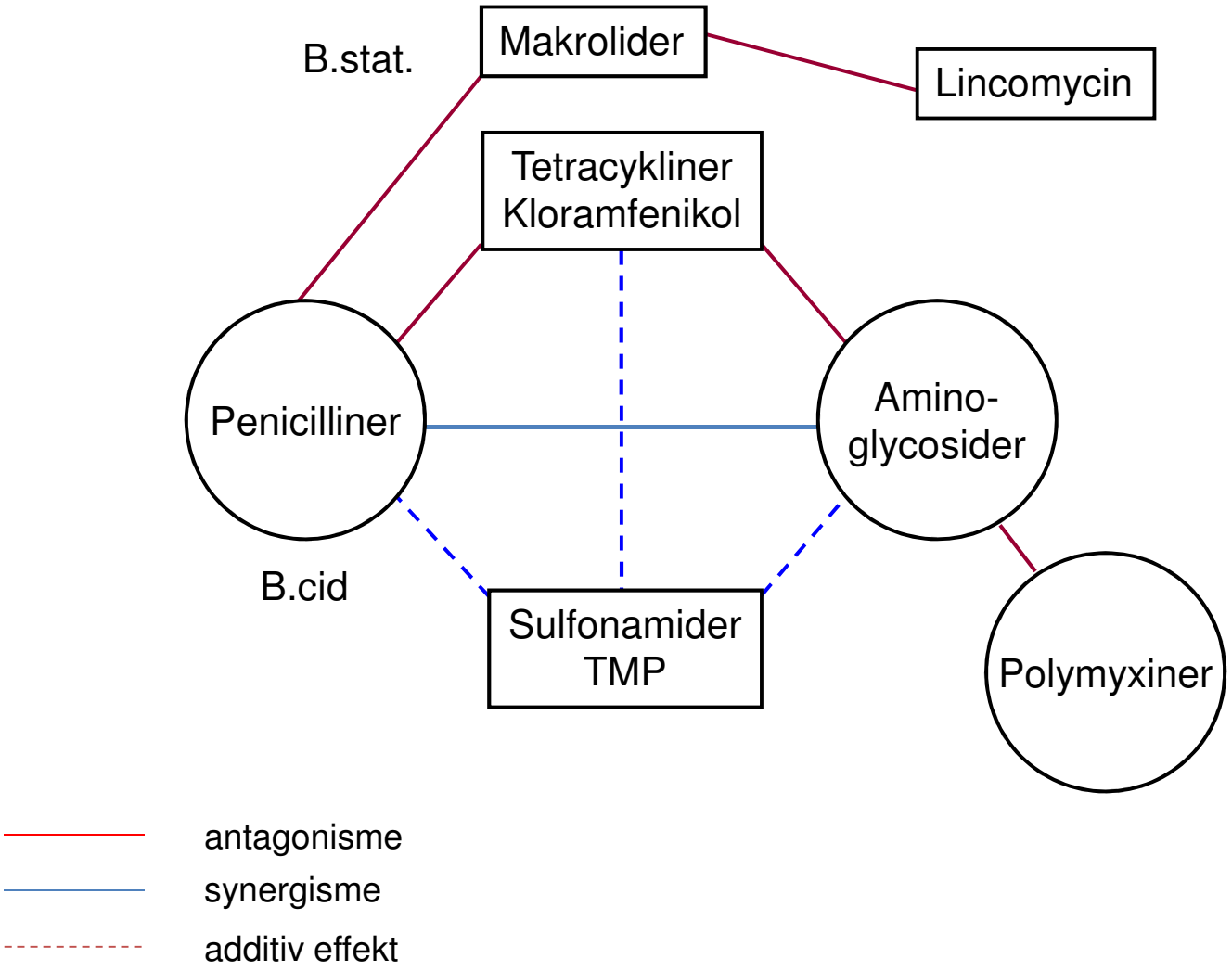
Postantibiotiske effekt

Relateret til:

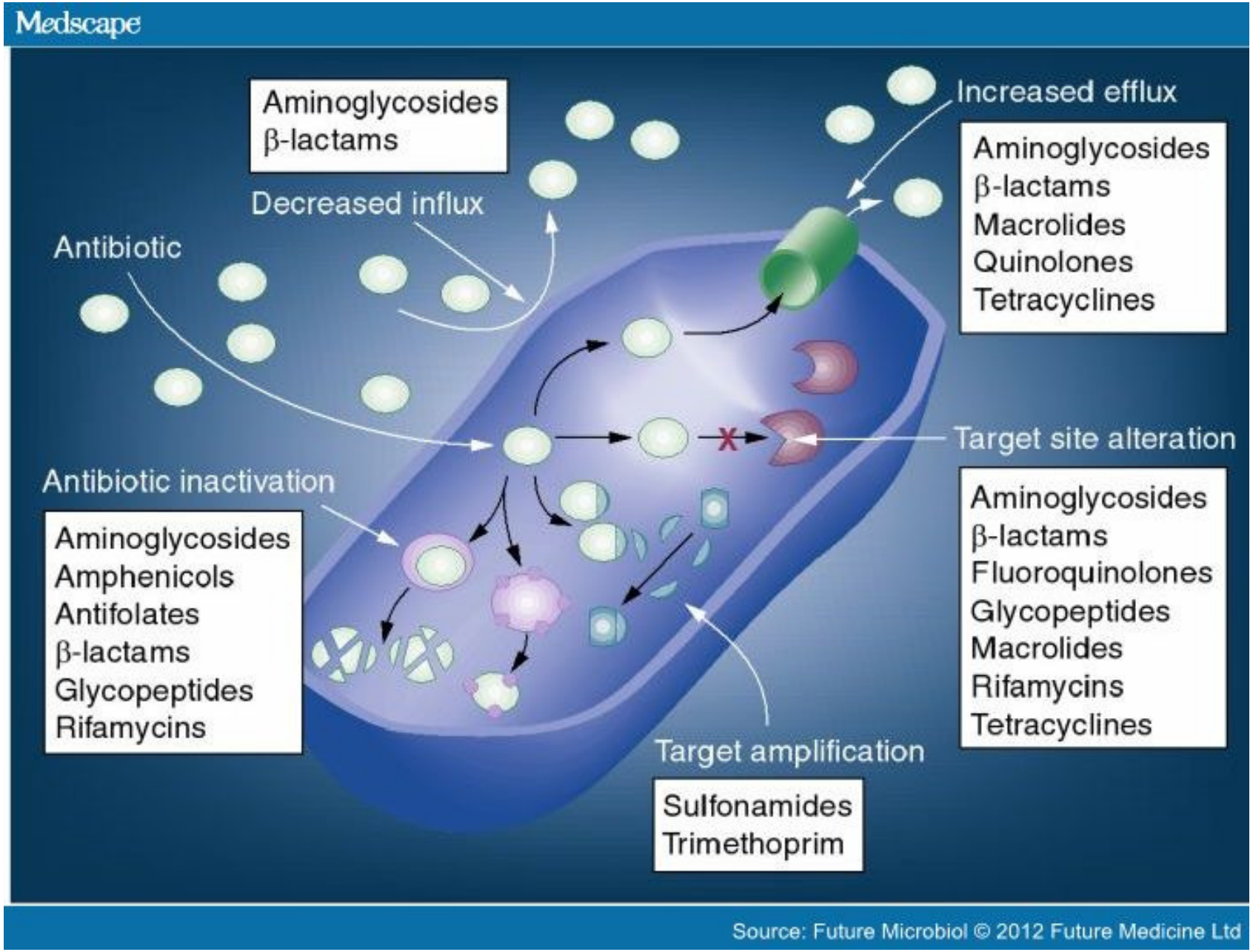
- Type af mikroorganisme og antibiotika
- Antibiotika koncentration
- Påvirkningstid


Neutral
Synergisme
Antagonisme
Antal
lev.
bakt.
K
B
A
A+B
K
B
A
A+B
K
B
A+B
A

Synergisme - Antagonisme



Resistensmekanismer

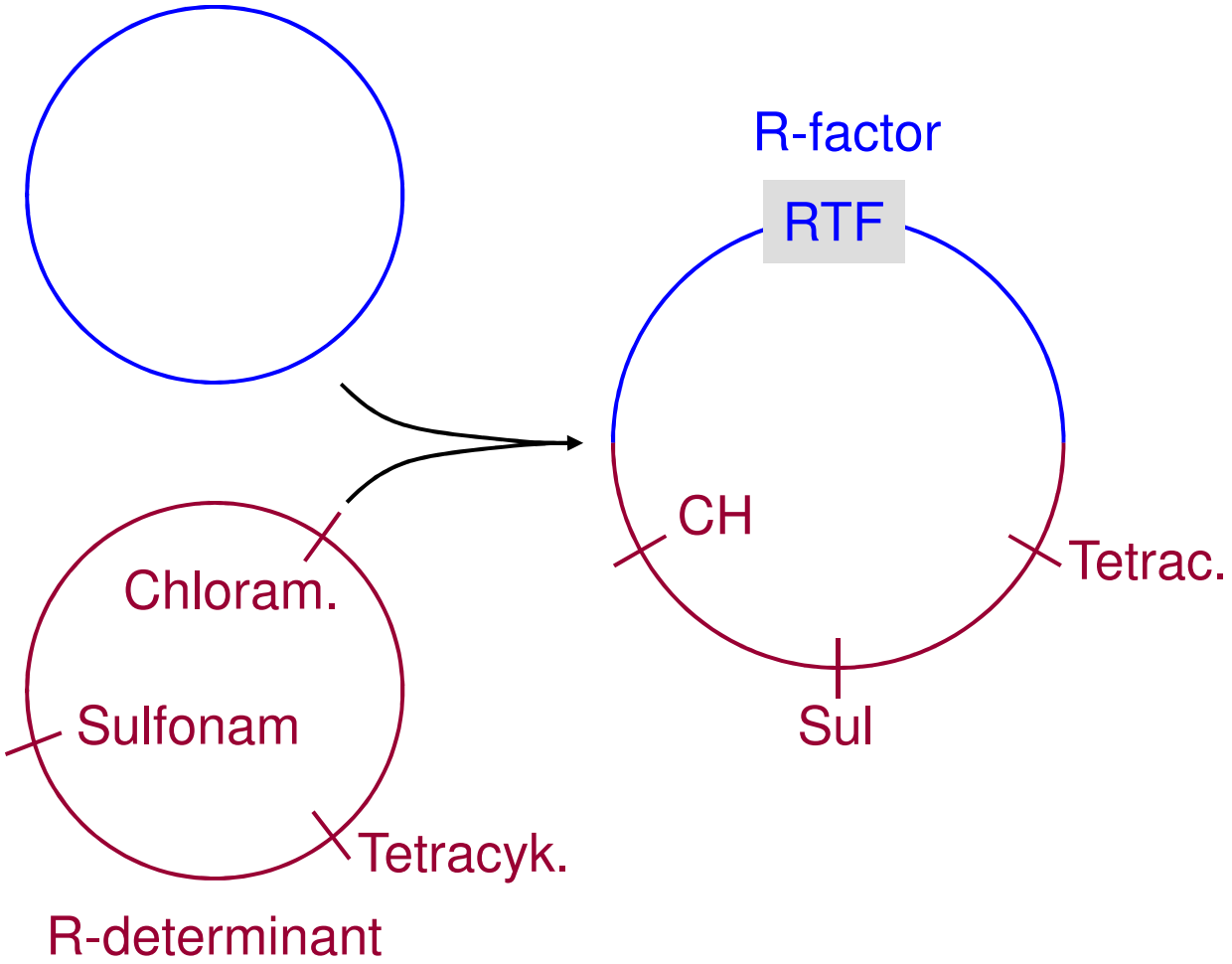


Resistens

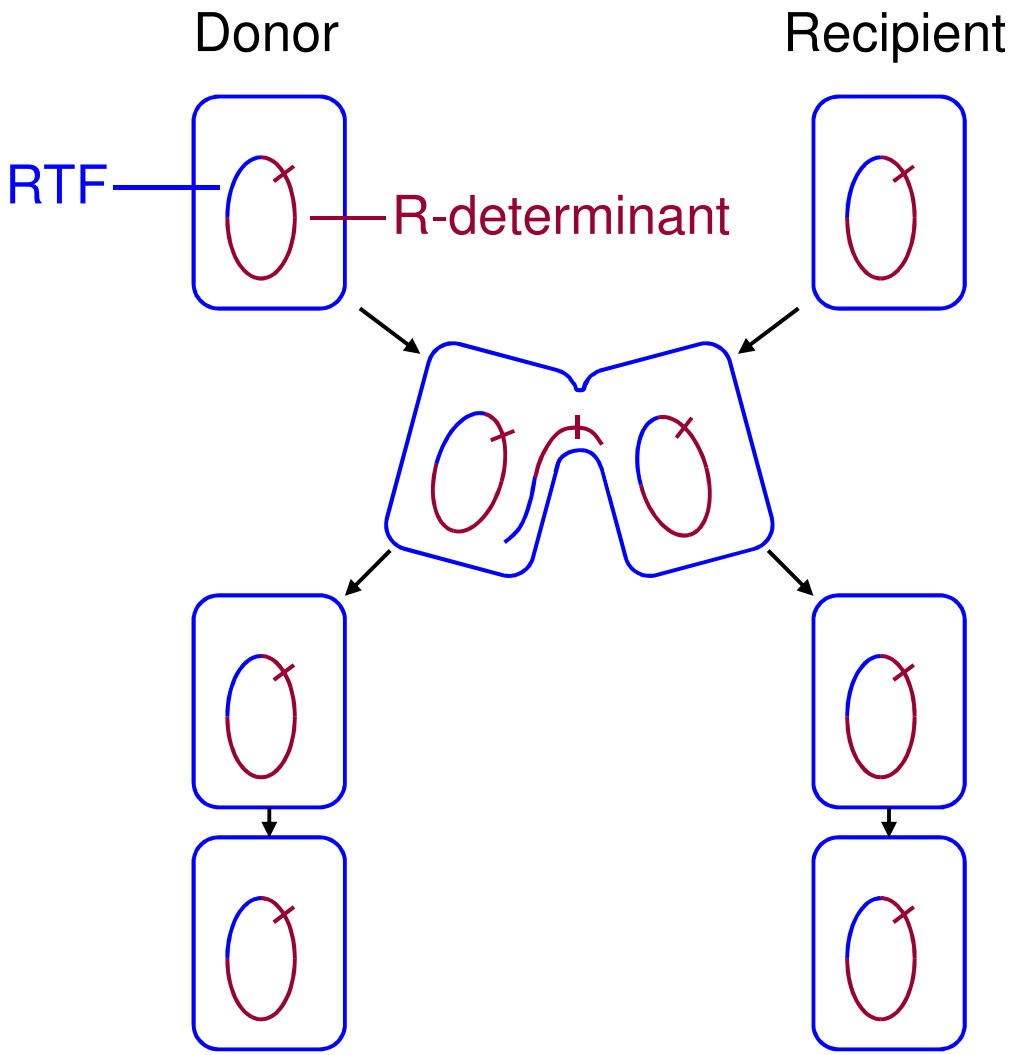
- Naturlig
- Erhvervet
  - a) mutation 10^{-7}-10^{-10}
    - ét trin
    - trinvis
  - b) overførsel
    - konjugation 10^{-2}-10^{-5}
    - transduktion 10^{-3}-10^{-6}

Resistensoverførsel - konjugation

R-Transfer Factor (RTF)

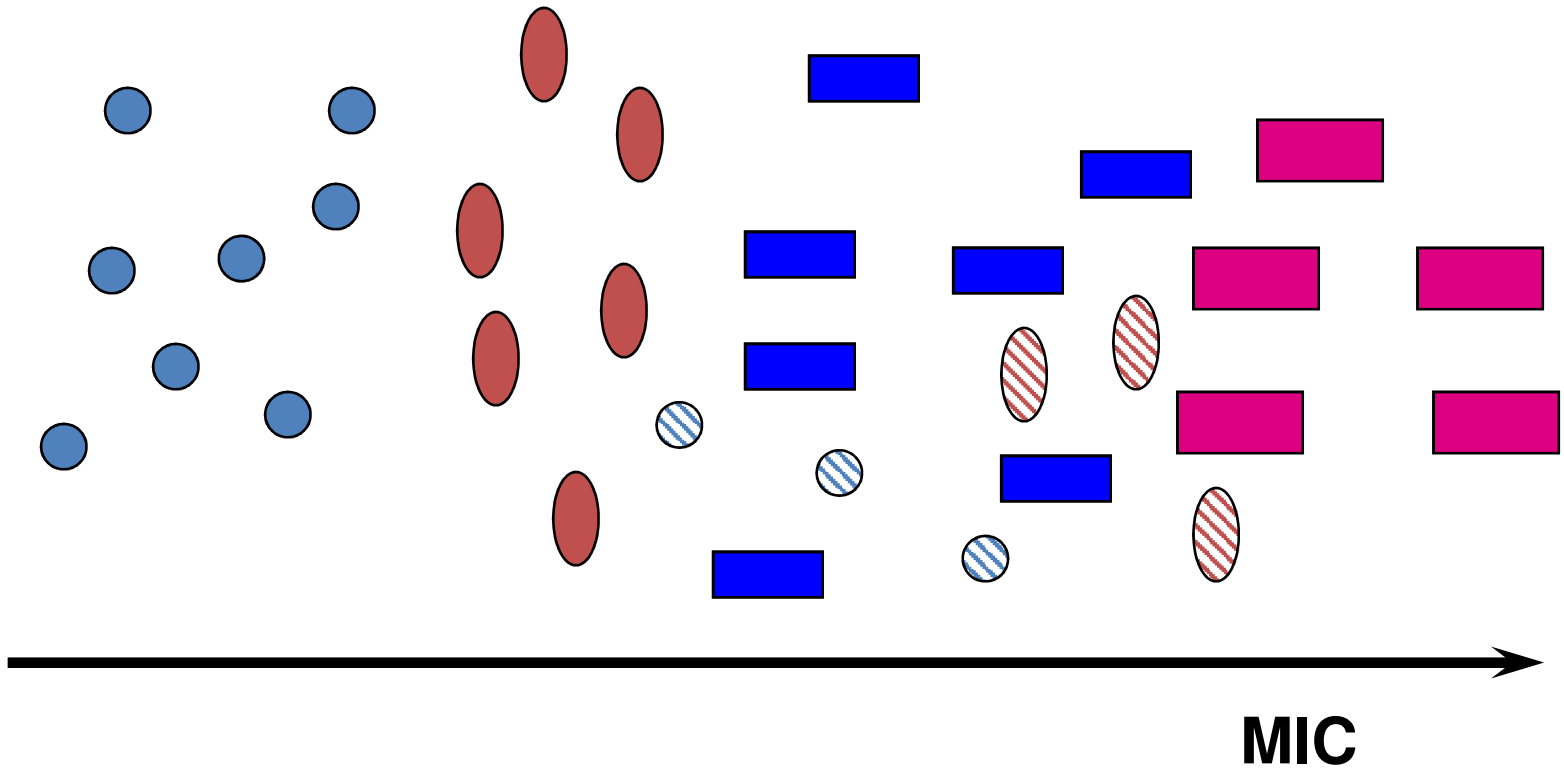


Resistensoverførsel - konjugation



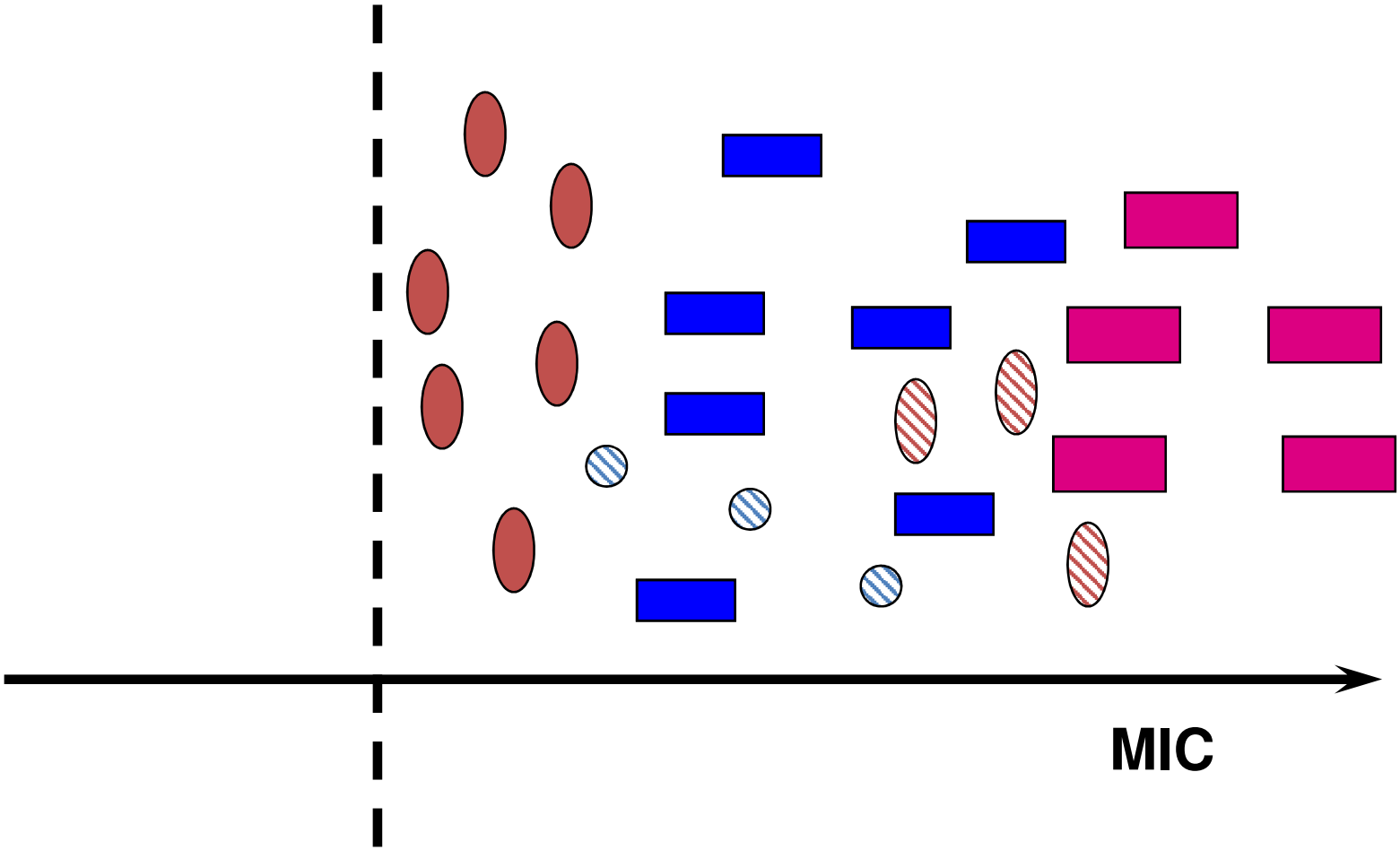
Development of resistance

Flora of the Gastro-Intestinal Tract



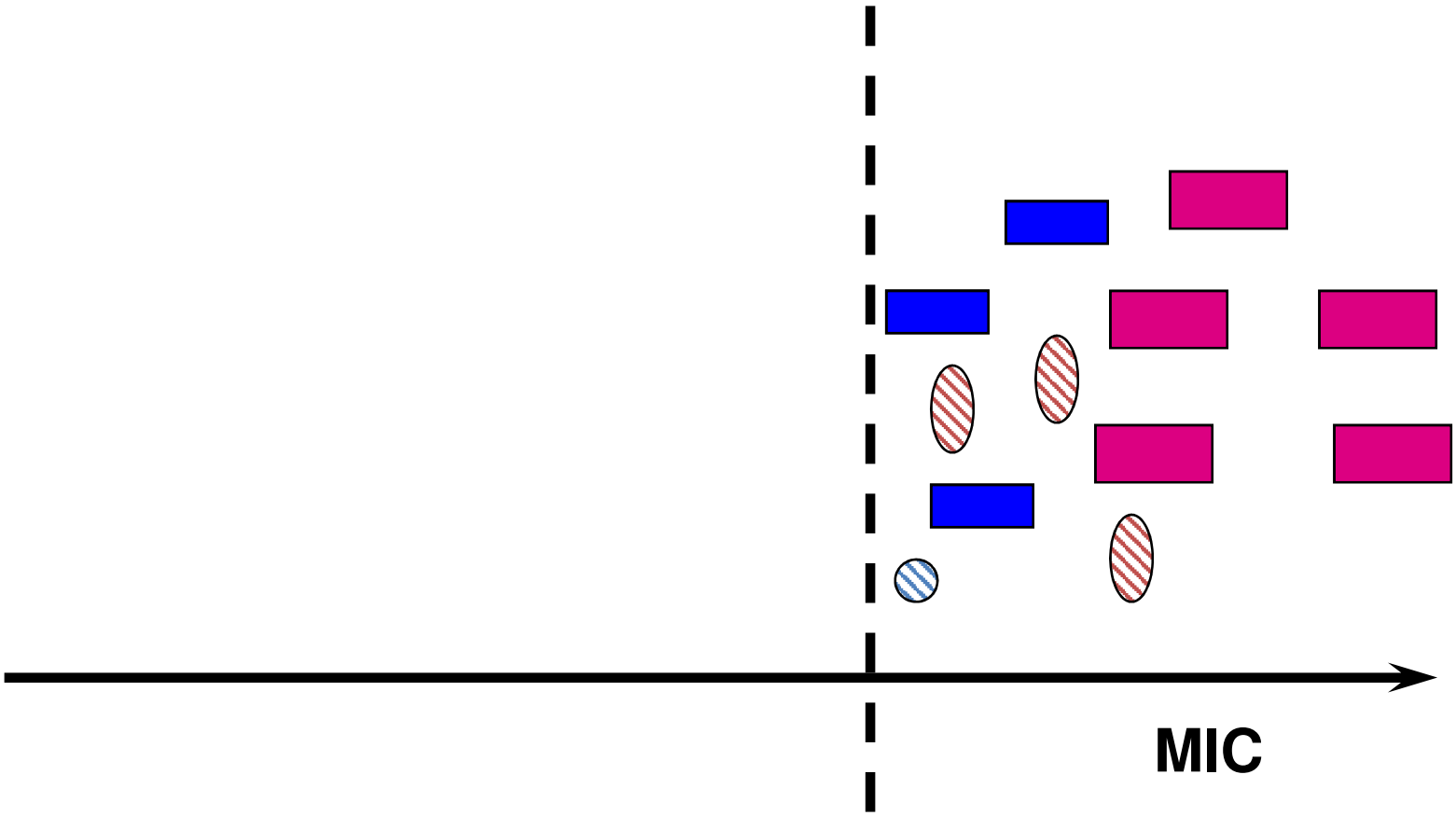
Development of resistance

Effect of a low dose



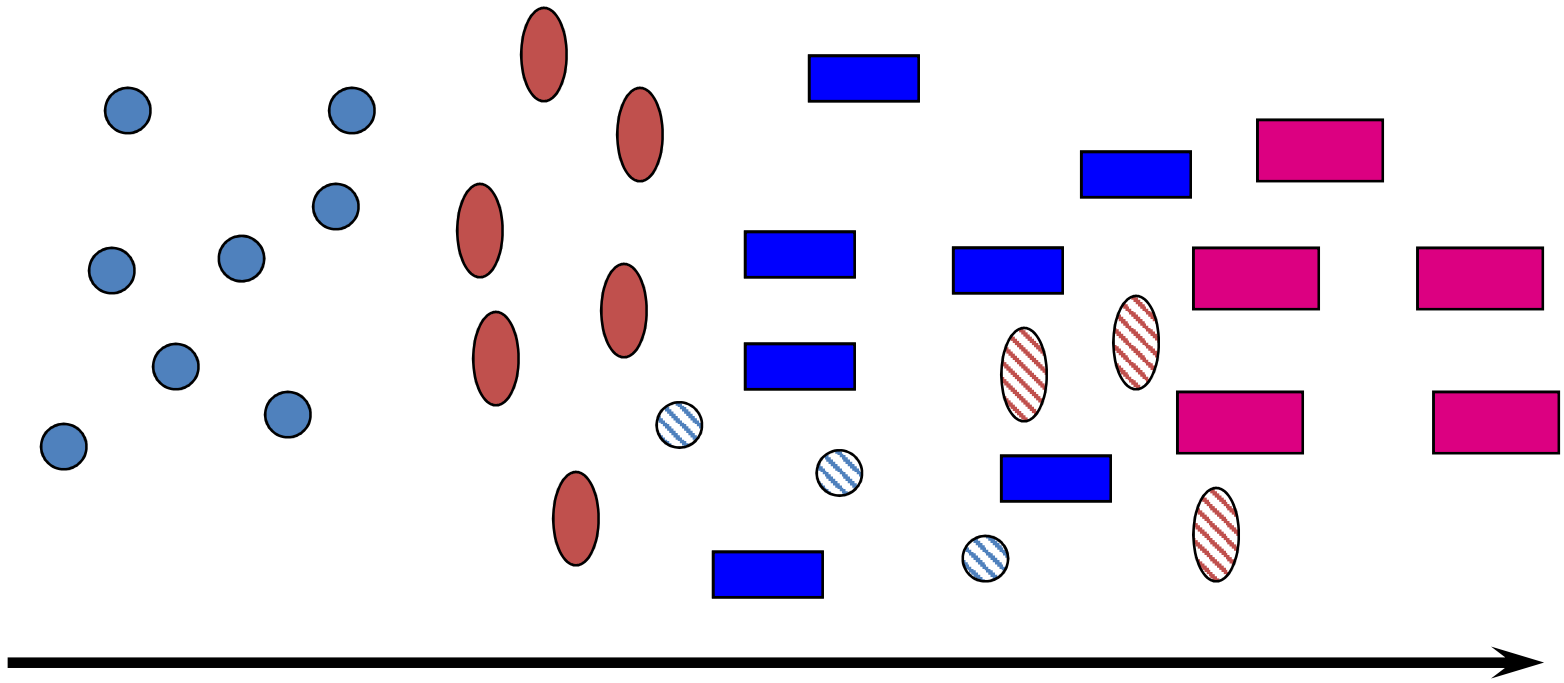
Development of resistance

Effect of a high dose



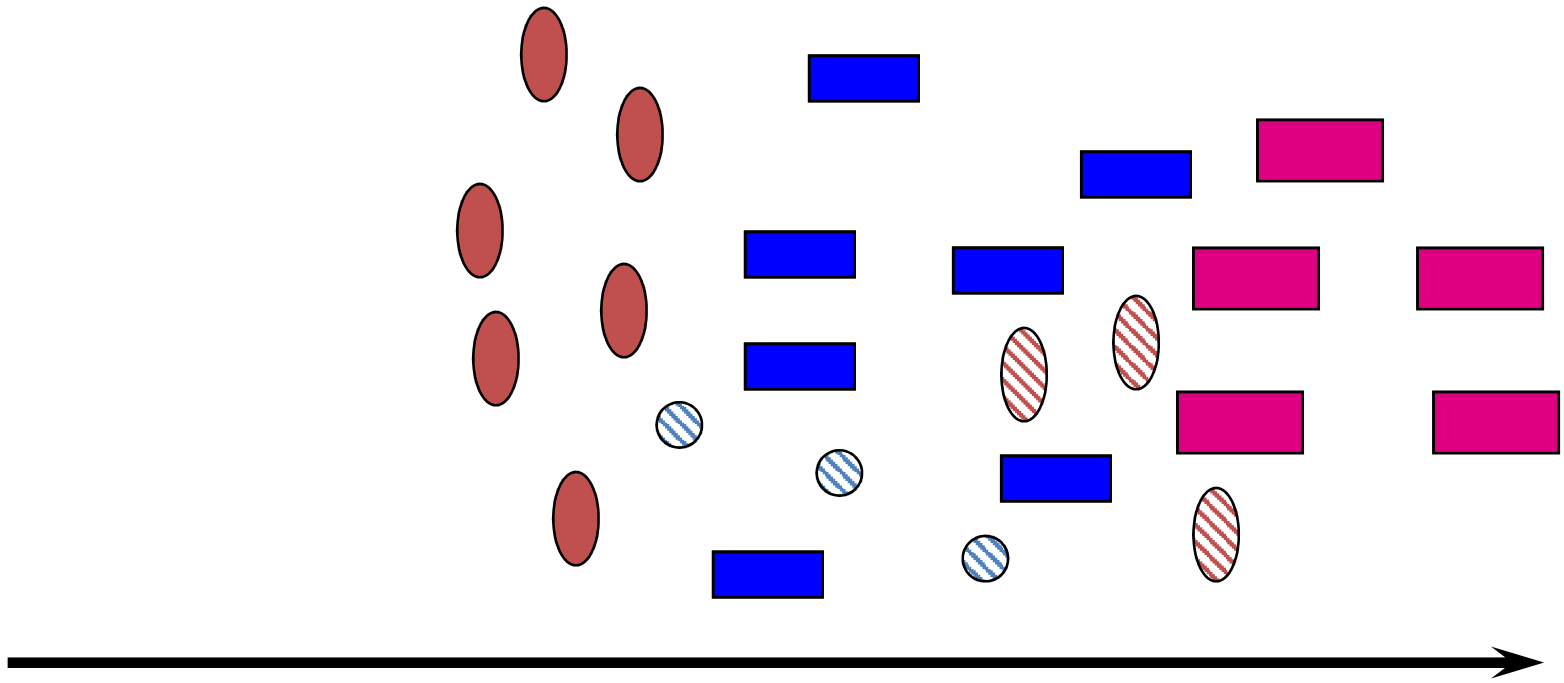
Development of resistance

Flora of the Gastro-Intestinal Tract



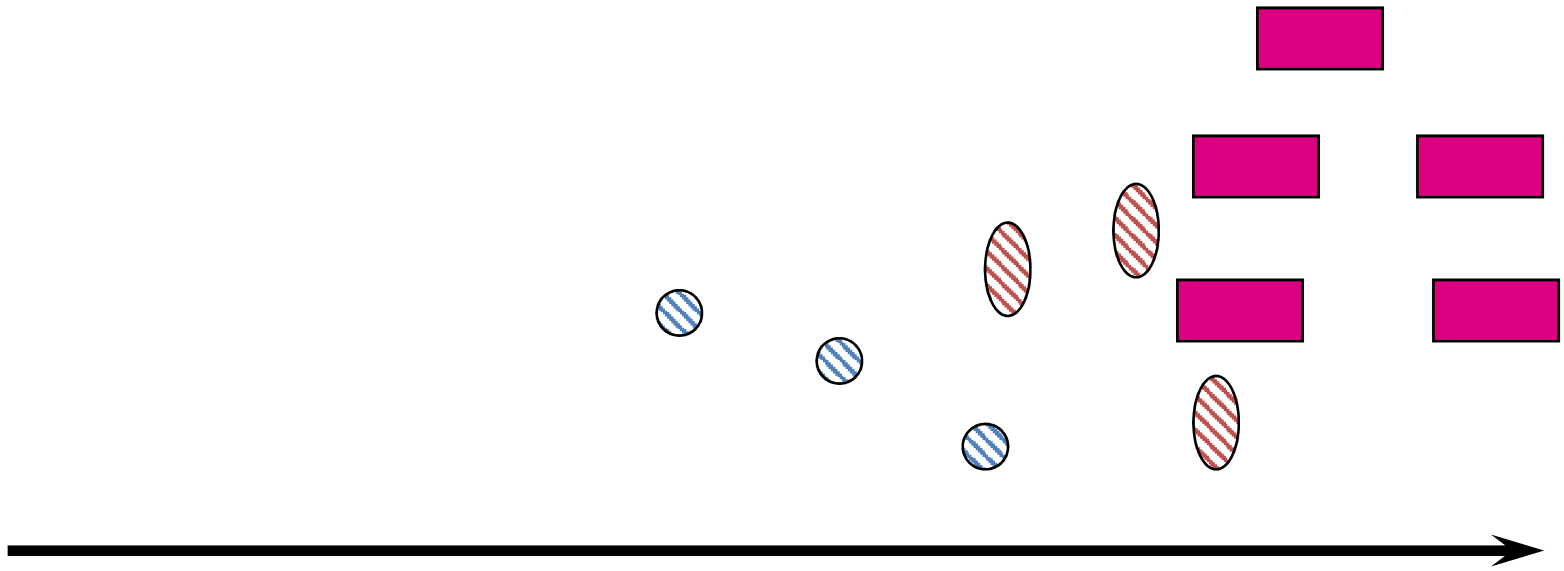
Development of resistance

Effect of a narrow spectrum antibiotic



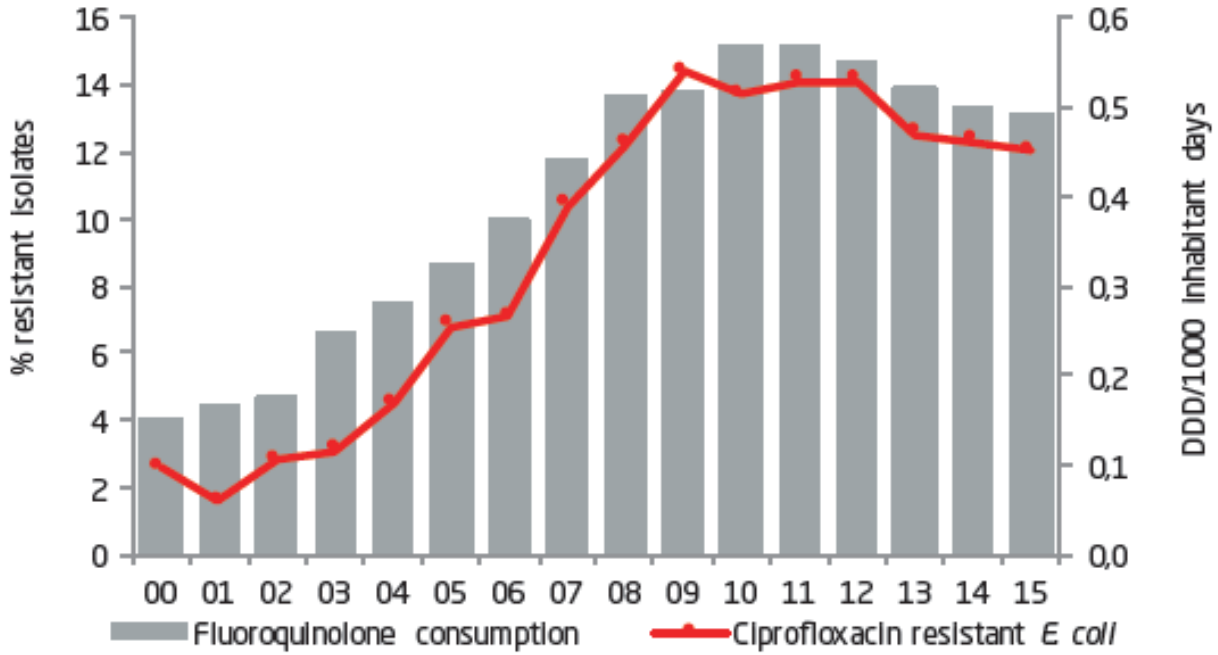
Development of resistance

Effect of a broad spectrum antibiotic

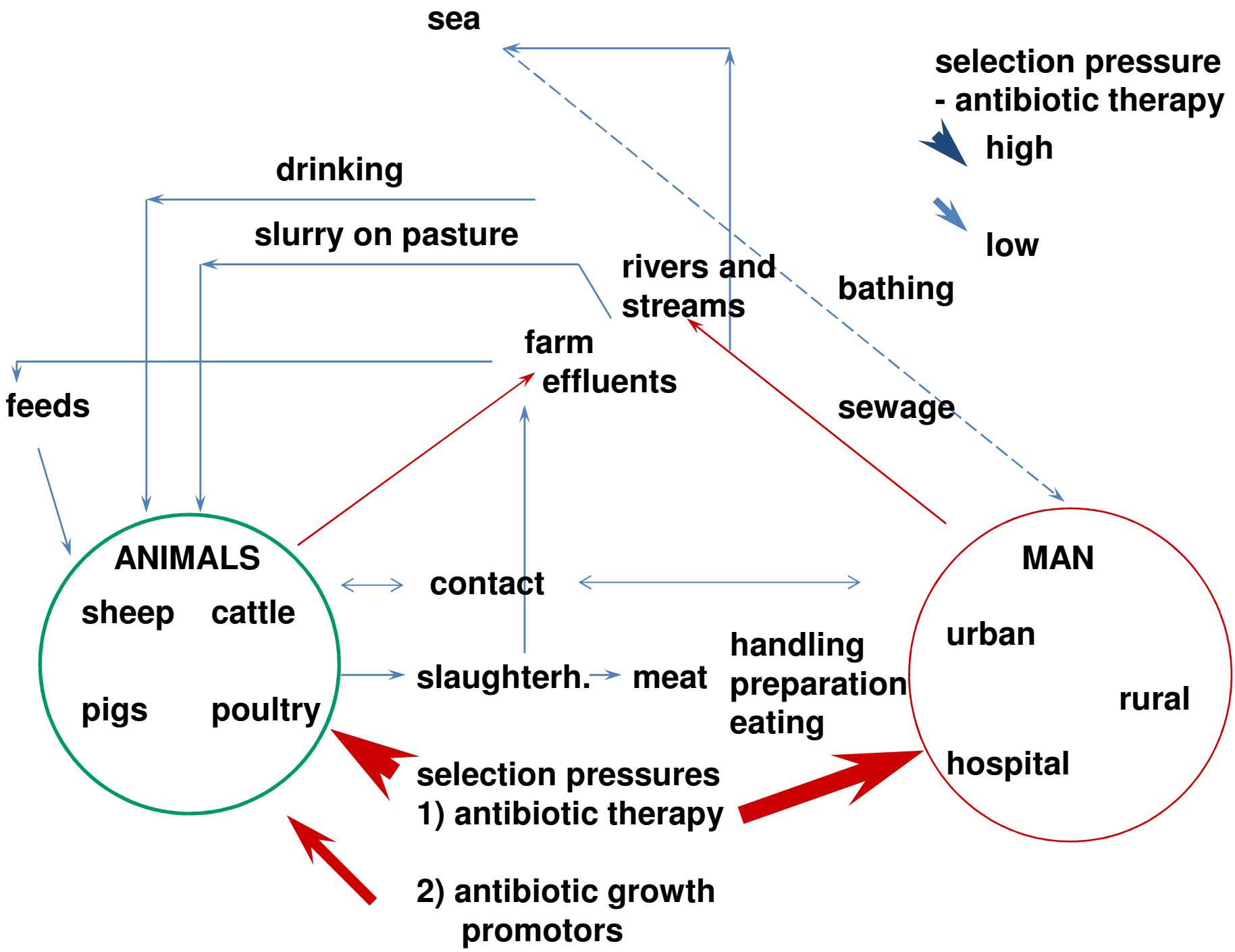


Forbrug vs resistens

Figure 2. Resistance (%) in *Escherichia coli* from urine samples and fluoroquinolone consumption, data from primary health care, Denmark



DANMAP 2015


sea
selection pressure
- antibiotic therapy
high
low
drinking
slurry on pasture
rivers and
streams
bathing
farm
effluents
feeds
sewage
ANIMALS
sheep
cattle
pigs
poultry
contact
slaughterh.
meat
handling
preparation
eating
MAN
urban
rural
hospital
selection pressures
1) antibiotic therapy
2) antibiotic growth
promotors

Bakterier, der hyppigt overfører resistens

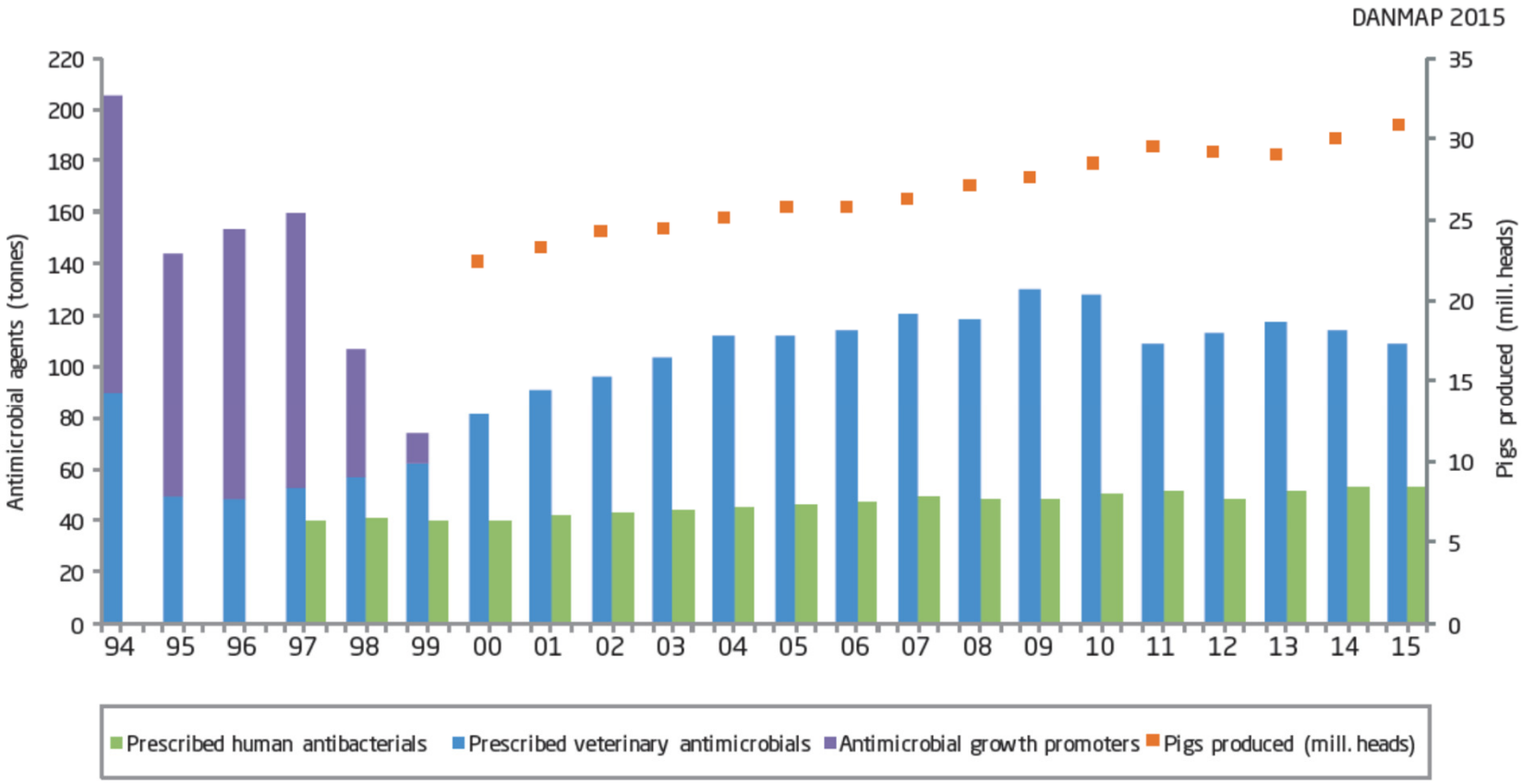
- Salmonella spp.
- E. coli
- Enterococcer
- Staphylococcer
- Campylobacter

Critically Important Antimicrobials for Human Medicine, 4th Revision 2013, WHO

- fluoroquinolones
- 3rd and 4th generation cephalosporins
- macrolides
- glycopeptides

C1: sole or limit alternatives C2: bacteria transmitted/acquire resistance genes from non-human sources

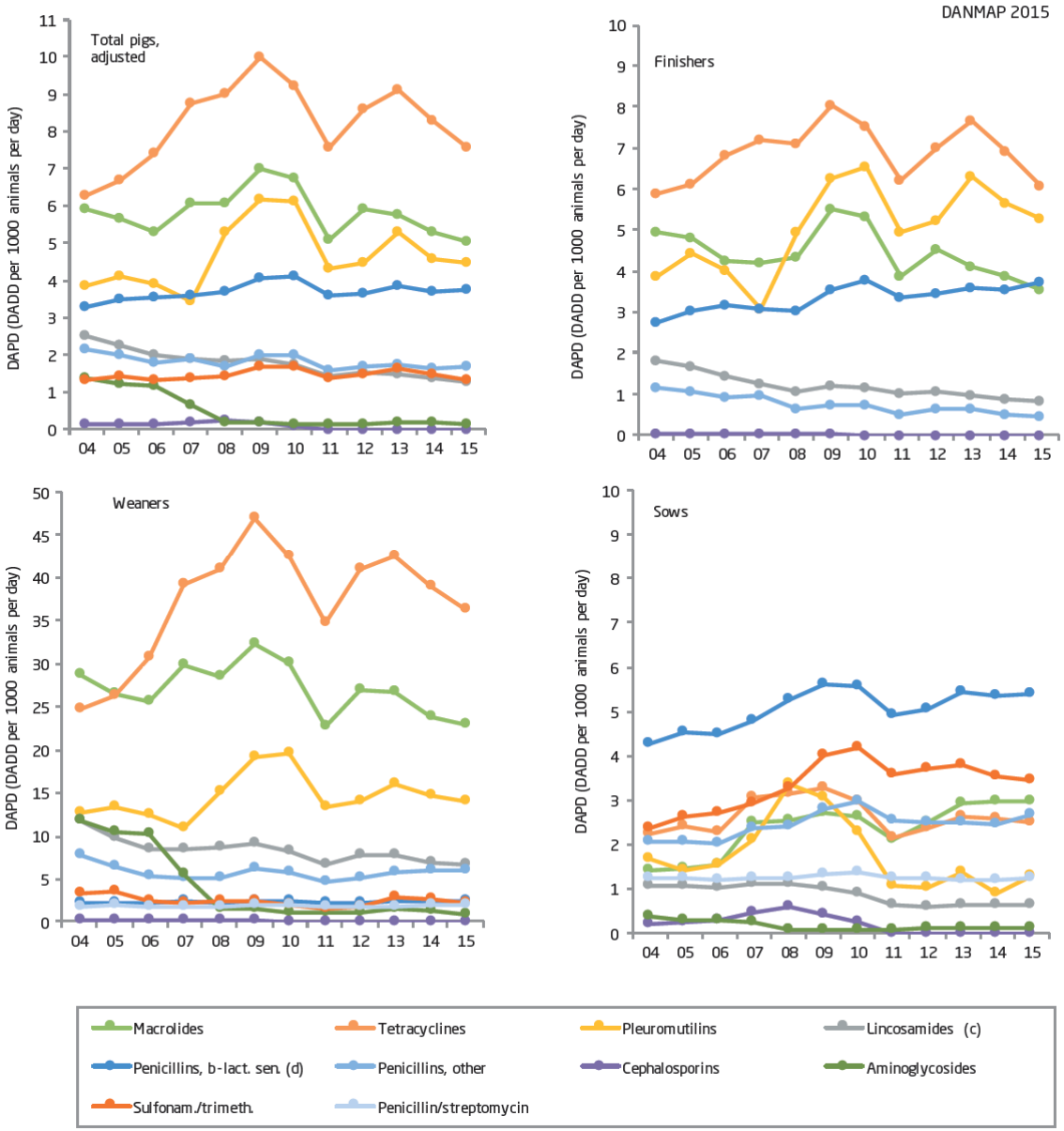
Consumption DK



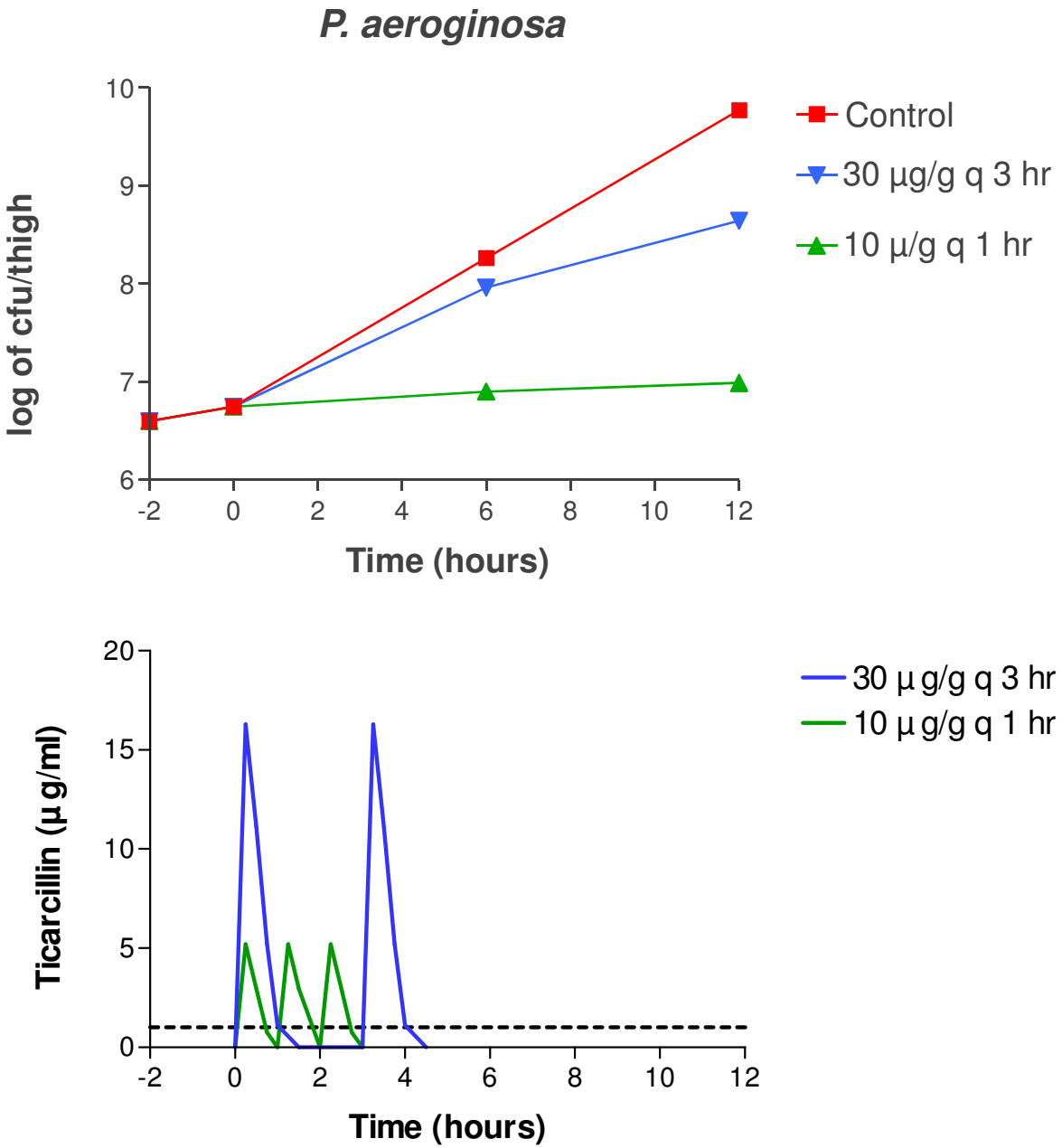
DANMAP 2015

Consumption pigs, DK

Figure 4.4. Antimicrobial consumption[a] in the total pig production[b], and in finishers, weaners, sows and piglets, Denmark

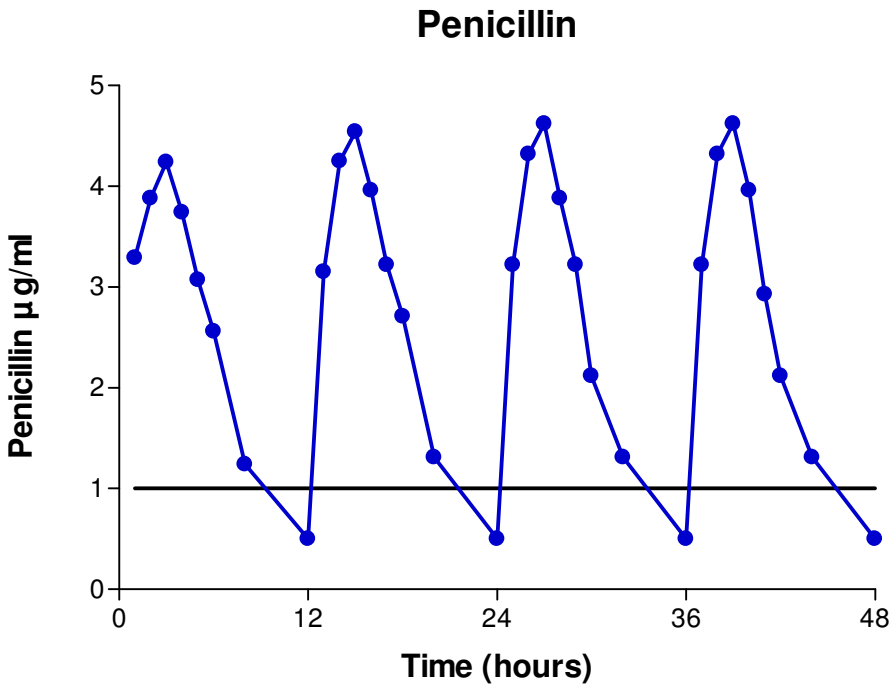


DANMAP 2015

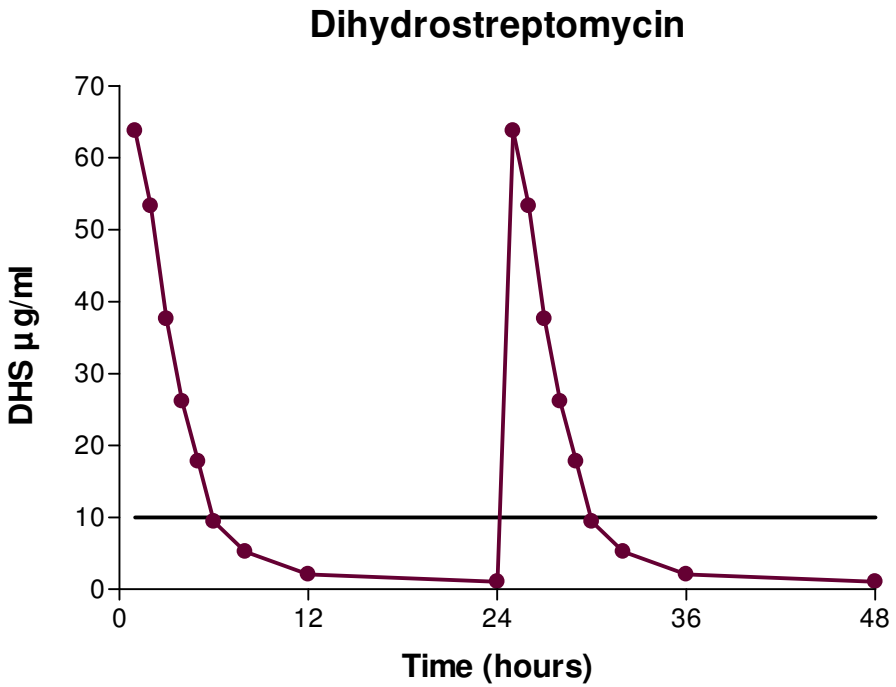

P. aeroginosa
log of cfu/thigh
10
9
8
7
6
-2
0
2
4
6
8
10
12
Time (hours)
Control
30 µg/g q 3 hr
10 µ/g q 1 hr
Ticarcillin (µ g/ml)
20
15
10
5
0
-2
0
2
4
6
8
10
12
Time (hours)
30 µ g/g q 3 hr
10 µ g/g q 1 hr

Ideal Concentration Profiles

Time dependent activity



Concentration dependent activity



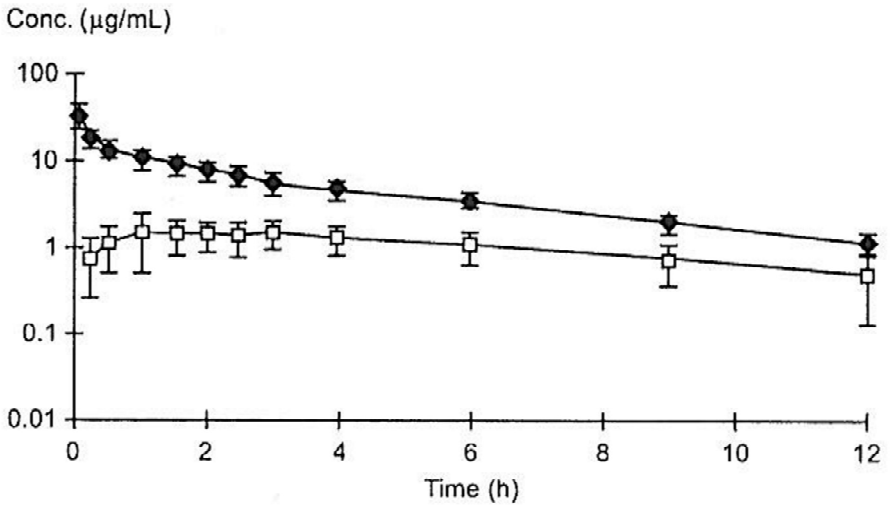
Dosing strategies

	Time dependent	Conc. dependent
Penicillins	X	
Aminoglycosides		X
Fluoroquinolones		X
Tetracyclines	X	
Macrolides	X	
Pleuromutilins	X	
Colistin		X

Doxycycline indications

- Swine respiratory disease
- Post weaning colibacillosis
  - *E. coli (K88)*
- Porcine proliferative enteritis
  - *Lawsonia intracellularis*

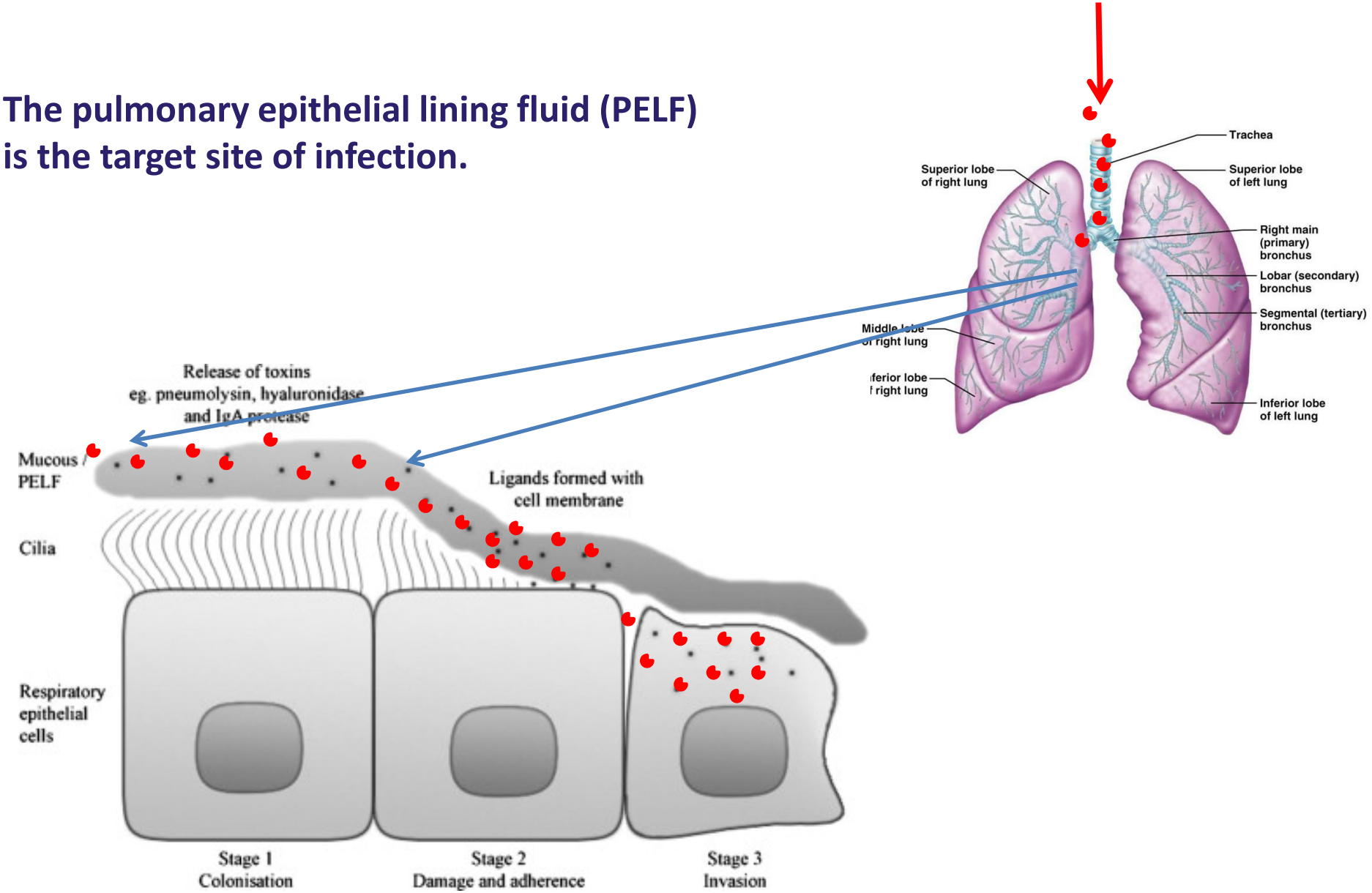
Doxycycline



	IV	PO
Dose, mg/kg	10	10
V, L/kg	0.8	
T½, h	4.2	2.9
Cmax, ug/ml		1.5
Tmax, h		2.3
F, %		21

Baert et al. J. vet Pharmacol. Therap. 2000, 23, 45-48

The pulmonary epithelial lining fluid (PELF) is the target site of infection.

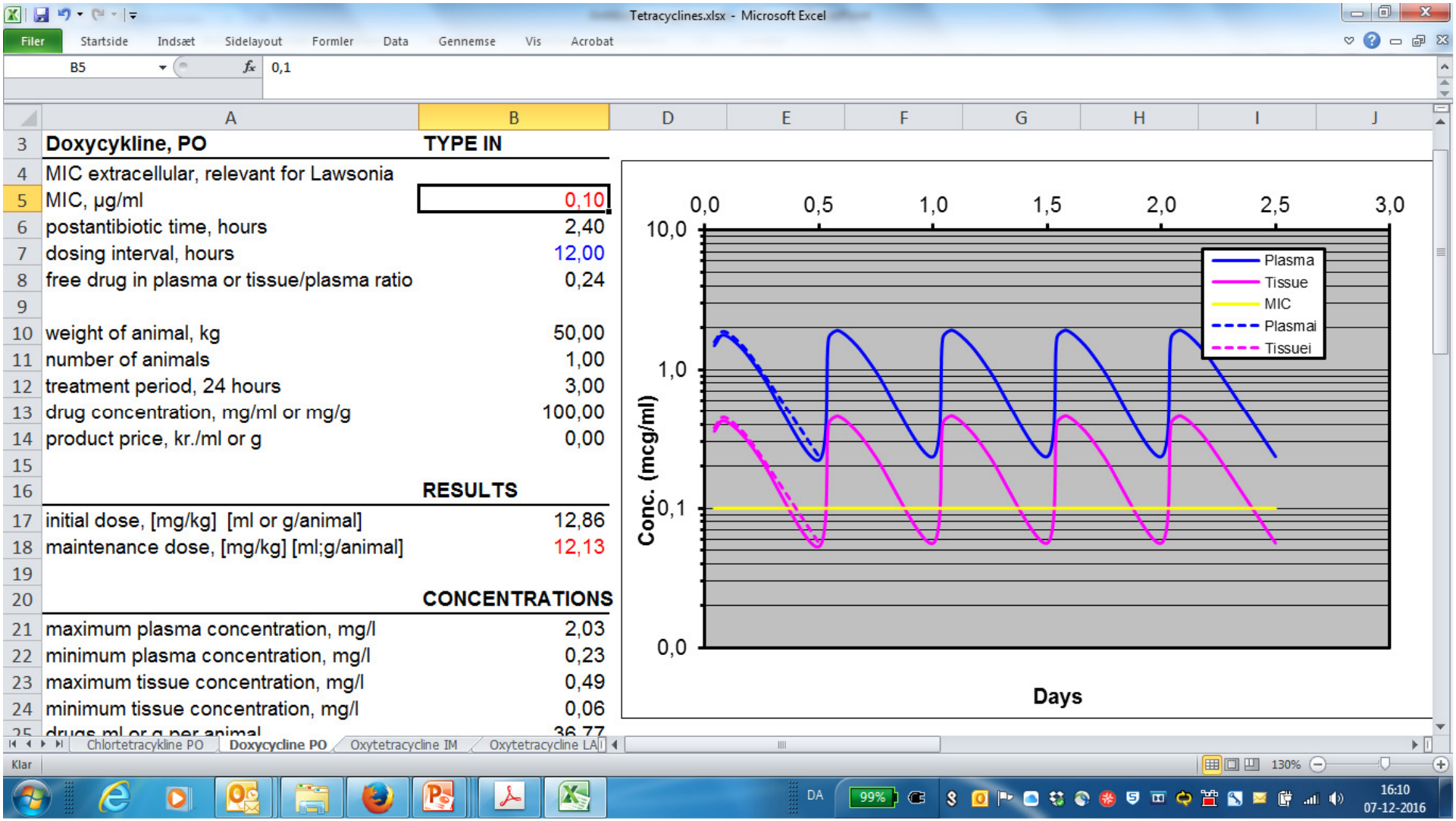


Tetracycline (MIC 4; 8)

Pathogen	MIC value	Number	Pct.	Pct.sum	MIC 50	MIC 90
APP	<=0,06	3	0,7	0,7		
	0,12	2	0,5	1,2		
	0,25	3	0,7	2,0		
	0,50	19	4,7	6,6		
	1,00	282	69,1	75,7	1,00	
	2,00	89	21,8	97,5		2,00
	8,00	2	0,5	98,0		
	16,00	5	1,2	99,3		
	>16,00	3	0,7	100,0		
		408	100,0			
P. multocida	<=0,06	1	0,7	0,7		
	0,25	2	1,4	2,1		
	0,50	91	65,0	67,1	0,50	
	1,00	38	27,1	94,3		1,00
	2,00	4	2,9	97,1		
	4,00	1	0,7	97,9		
	16,00	3	2,1	100,0		
		140	100,0			

Danish Veterinary Institute 2006-2008

Doxycycline po, luftvejsinfektion



Doxycycline po, luftvejsinfektion